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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/922,240	08/27/1997	STUART L. SCHREIBER	APBI-P01-007	1342

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EXAMINER
SHUKLA, RAM R

ART UNIT	PAPER NUMBER
1632	32

DATE MAILED: 07/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/922,240	SCHREIBER ET AL.	
	Examiner	Art Unit	
	Ram R. Shukla	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-16,18-26,29,32,33,36,38,39,44 and 45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-16,18-26,29,32,33,36,38,39,44 and 45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 October 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Receipt is acknowledged of a request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e) and a submission, filed on 4-2-03.

2. Applicant's amendments and response filed 4-2-03 have been entered. Applicants after final amendment filed 9-27-02 has been entered.

3. New claim 45 has been added.

4. Claims 1, 4-16, 18-26, 29, 32-33, 36, 38-39 and 44-45 are pending.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claim 1, 4-15, 16, 18-26, 29, 39 and 45 remain rejected under 35 U.S.C. 112, first paragraph, for reasons of record set forth in the office actions of 3-27-02 because the specification, while being enabling for an in vitro method of preferentially inhibiting proliferation of T cells or an ex vivo method of preferentially inhibiting proliferation of genetically engineered T cells in an animal, wherein in the ex vivo method introduced cells are autologous or allogeneic to the animal and wherein the mutated MBP in the in vitro or ex vivo methods have characteristics as recited in claim 1b and 1c, does not reasonably provide enablement for any other recited embodiments. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

It is emphasized that claims 16 is enabled for the scope stated above to the extent it encompasses the mutated MBPs recited in claim 1 with the characteristics recited in claim 1b and 1c.

Response to Arguments

Applicant's arguments filed 4-2-03 and 9-27-02 have been fully considered but they are not persuasive. Applicants' arguments A and B are moot in view of the new scope rejection indicating ex vivo method or in vitro method enabled. Regarding claim 26, it is noted that the ex vivo method is enabled for autologous or allogeneic cells only. Finally, applicants' arguments in paragraph C are not persuasive because applicants discussed the issue of macrolide administration only and did not address the issue of administering the nucleic acid that encodes the mutated MBP. As instantly recited claims 1, 4-15 and 45 encompass an in vivo method wherein the nucleic acid encoding a mutated MBP as recited is administered to T cells in an animal by any route using any vector. While progress has been made in recent years for *in vivo* gene transfer, vector targeting *in vivo* to desired organs or cells continues to be unpredictable and inefficient. This is supported by numerous teachings available in the art. For example, Miller et al. reviews the types of vectors available for *in vivo* gene therapy, and conclude that "for the long-term success as well as the widespread applicability of human gene therapy, there will have to be advances...targeting strategies outlined in this review, which are currently only at the experimental level, will have to be translated into components of safe and highly efficient delivery systems" (page 198, column 1). Deonarain is a 1998 publication which indicates that one of the biggest problems hampering successful gene therapy is the "ability to target a gene to a significant population of cells and express it at adequate levels for a long enough period of time" (page 53, first paragraph). Deonarain reviews new techniques under experimentation in the art which show promise, but is currently even less efficient than viral gene delivery (see page 65, first paragraph under Conclusion section).

Claim Rejecti ns - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 32, 33 and 44 are rejected under 35 U.S.C. 102(b) as being anticipated by Futer et al (The Journal of Biological Chemistry 270:18935-18940, 1995).

Futer et al teaches mutational analysis of FK506 binding protein and characterization of the mutants by studying drug binding and enzymatic activities (see figures 1 and 3 and table 1). It is noted that while the art does not teach inhibition of proliferation, such a property will be inherent to the mutants that have altered drug binding and enzymatic activity. Since the art teaches both the MBP and the macrolide, it encompasses the kit recited in claim 33.

9. Claims 32, 33 and 44 are rejected under 35 U.S.C. 102(b) as being anticipated by Kawamura et al (The Journal of Biological Chemistry 270:15463-15466, 1995).

Kawamura et al et al teaches mutational analysis of FK506 binding protein and characterization of the mutants by studying drug binding and enzymatic activities (see figures 2 and 3 and table 1). It is noted that while the art does not teach inhibition of proliferation, such a property will be inherent to the mutants that have altered drug binding and enzymatic activity. Since the art teaches both the MBP and the macrolide, it encompasses the kit recited in claim 33.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 32, 33, 36, 38 and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Futer et al (The Journal of Biological Chemistry 270:18935-18940, 1995) or Kawamura et al (The Journal of Biological Chemistry 270:15463-15466, 1995) in view of Fruman et al (Molecular and Cellular Biology 15:3857-3863, 1995).

Futer et al teaches mutational analysis of FK506 binding protein and characterization of the mutants by studying drug binding and enzymatic activities (see figures 1 and 3 and table 1). Futer et al does not teach a method of genetically engineering T cells comprising mutant MBP of claim 32or a population of cells comprising T cells comprising the mutant MBP of claim 32.

Kawamura et al et al teaches mutational analysis of FK506 binding protein and characterization of the mutants by studying drug binding and enzymatic activities (see figures 2 and 3 and table 1). Kawamura et al does not teach a method of genetically engineering T cells comprising mutant MBP of claim 32or a population of cells comprising T cells comprising the mutant MBP of claim 32.

Fruman et al teaches characterization of Mutant Calcineurin Aα gene in EL4 lymphoma cells and Jurkat T cells (see the materials and methods section).

At the time of the invention, it would have been obvious to an artisan of ordinary skill to make T cells comprising mutant MBP by modifying the

method of Fruman et al and using the nucleic acids taught by Futer et al or Kawamura et al with a reasonable expectation of success. An artisan of skill would have been motivated to make such T cells because this would have allowed in characterizing the function of the mutant MBPs in cells and confirm the results obtained in vitro in enzyme assays and drug binding assays.

12. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (703) 305-1677. The examiner can normally be reached on Monday through Friday from 7:30 am to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The fax phone number for this Group is (703) 308-4242. The after-final fax number is (703) 87209307. Any inquiry of a general nature, formal matters or relating to the status of this application or proceeding should be directed to the William Phillips whose telephone number is (703) 305-3413.

RAM SHUKLA
PRIMARY EXAMINER

Ram R. Shukla, Ph.D.
Primary Examiner
Art Unit 1632